UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

PURDUE PHARMA L.P., et al.,

Plaintiffs,

v.

ENDO PHARMACEUTICALS, INC.,

Defendant.

Trial

00 Civ. 8029 (SHS)
01 Civ. 2109 (SHS)
01 Civ. 8117 (SHS)

New York, N.Y.
June 2, 2003
10:00 a.m.

Before:

HON. SIDNEY H. STEIN

District Judge

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(Case called)

THE COURT: Good morning all. This is the trial of Purdue v. Endo, three cases, 00 Civ. 8029, 01 Civ. 2109, and 01 Civ. 8117.

I would like to handle some housekeeping matters first. The first thing, I believe I made this disclosure at the very first time we met. But just so the record is completely clear, and it is a disclosure I made at the trial of the prior case as well, an employee of Purdue Pharma formerly was an associate at my former firm, then known as Stein Zauderer Ellenhorn Frischer & Sharp. He left Stein Zauderer before I did, so my guess is that was at least ten years ago. His name is Richard Silber. I believe he is still an employee, he is an attorney, an employee of Purdue Pharma.

I can adopt the matters that the parties have arrived at and agreed to in the letters dated May 23 and May 31, which really are procedural matters. The May 23rd letter is from Mr. Schwartz, setting forth the fact that cross won't be limited to the scope of direct where the person would have been called by the other side. Then, no need for a subpoena for the production of employees and agents of the parties, and so forth. I have no problem with that.

Similarly, I have copies of letters dated May 30 and May 31, which really are letters between counsel, but they set forth agreements on similar matters, and I have no problem with

THE COURT: Wait just a moment.

MR. FLATTMANN: Certainly.

THE COURT: I understand. You are talking about OxyContin. You aren't referring to the drug oxycodone but to the product, the commercial product OxyContin?

THE WITNESS: Yes.

THE COURT: All right.

Q. What effect would increasing the amount of oxycodone in the combination products have on the duration of pain relief that they afford?

A. Really very little effect. It might increase the duration a half hour or so, but not beyond that four to six-hour period.

Q. Why is that?

A. Because it is formulated in immediate-release formulations. The drug is released from the formulation and the duration is short.

Q. Now let me ask you a different question. What effect would increasing the amount of either aspirin or acetaminophen in these combination products have on the duration of pain relief that they afford?

A. Again, it might increase the duration marginally, but again not beyond six hours or so.

Q. Would increasing the amount of aspirin or acetaminophen in these combination products have any other effects?

A. Potentially, yes. These drugs, aspirin and acetaminophen

have maximum or ceiling dosages that are safe to give in a 24-hour period, particularly when patients take these medications on a 24-hour basis.

Q. Why do they have ceiling dosages?

A. It is a property of their pharmacology, that there is just a dose that you can't go beyond and get additional analgesia, or pain relief.

Q. What happens if you go beyond the ceiling dose?

A. If you go beyond the ceiling dose, you don't get any benefit in terms of increasing the analgesia. You may get a slight benefit of duration. But you can put the patient at risk for kidney or liver toxicity if they take the drugs over many days or weeks.

Q. Does OxyContin have any effect on the liver or kidneys?

A. No.

Q. Let me ask you to please turn to your next graphic. You made reference to that this case relates to controlled-release oxycodone formulations that produce certain blood plasma concentrations of the drug at certain times. Let's start with the term "blood plasma." What is blood plasma?

A. "Blood plasma" refers to the liquid portion of the blood.

Q. How are blood plasma concentrations of a drug described?

A. They are described in units of concentration typically, like milligrams per milliliter or nanograms per milliliter, those names.

Q. Let me ask you to please turn to your next graphic. What are you depicting here?

A. I am attempting to define the medical term "pharmacokinetics." One way to think about that is it is what the body does to the drug. A more precise definition is that pharmacokinetics is the blood plasma concentration of the drug in the body over time.

Q. You used the abbreviation "PK" on the chart. What does that stand for?

A. "PK" stands for pharmacokinetics.

Q. Let me ask you to please turn to your next graphic. Dr. Payne, what are you showing here?

A. An attempt to show the release of drug from a controlled-release formulation as it moves through the gastrointestinal tract.

Q. Could you show the video you prepared.

A. Yes. As the pill moves from the esophagus into the stomach, it begins to be absorbed, and the blue dots represent drug coming out of the formulation. It then moves from the stomach into the small intestinal tract. Again, the drug is released from this formulation slowly. Then, finally, the drug will move from the small intestine to the large intestine, and drug continues to be released from the formulation. So there is a continuous slow release of drug from the intestinal tract, from the stomach through the large intestine.

and I had the opportunity to be part of it and I became part of it.

Q. What did you do after you completed your post-doc?

A. Well, things were really kind of just a flow over a period of years, working with the post-doctorate program for a couple of years while setting up a laboratory in Memorial Sloan-Kettering. And then, after a few years, while still maintaining the laboratory, I became much more involved in clinical studies, their design and analysis and oversight and reporting of the clinical studies that the group was doing over the period of that decade.

Q. What was the general subject matter of your studies at Sloan-Kettering?

A. These were efficacy studies, where we looked at the potency of various analgesics, we looked at their onset, the duration of effect. We looked at the blood levels of analgesics. We tried to relate blood levels to effect. I also spent some considerable time looking back at studies that had been done before I got there, as well as working with the ongoing clinical research program.

Q. What analgesics did you work with primarily at Sloan Kettering?

A. We worked with quite a few, both directly and indirectly. I don't know that I could count them on two hands or three hands or four hands. Most often, a new analgesic would be

compared in our studies to morphine. So I guess in a way I learned more about morphine than I did any other particular analgesic that we were testing relative to morphine.

Q. Have you authored or co-authored any published papers about the treatment of pain?

A. Yes, I have.

Q. Approximately how many?

A. Nearly a hundred full manuscripts and nearly 200 abstracts of studies.

Q. Are you a named inventor on any patents besides the three patents in suit?

A. Yes, I am.

Q. Approximately how many?

A. I think about ten patents in addition to the three patents in suit.

Q. Do any of these patents involve advances in pain management?

A. Yes. They all do.

Q. When did you leave Sloan-Kettering?

A. I left Sloan-Kettering in September of '85.

Q. What did you do after you left?

A. I joined Purdue.

Q. What was your job title when you first went to Purdue?

A. Associate medical director.

Q. What were your responsibilities as associate medical

director?

A. My initial responsibilities when I just joined Purdue was to oversee the clinical research activities involving the currently marketed opioid analgesics -- analgesics in general rather. I participated in medical education activities, particularly lecturing, and I also had responsibility for responding to medical inquiries from health professionals who were called in or wrote in with questions about pain management or analgesics.

Q. Has your job changed over time?

A. My job changed to some extent. My responsibilities for clinical research went beyond analgesics into most of other areas that we were involved in. By 1990 I had responsibility for, as the vice president of clinical research, most all of the clinical research program.

Q. What products, if any, did you have responsibility for when you first arrived at Purdue?

A. When I very first arrived, I had responsibility for MS Contin and another analgesic, a nonopioid analgesic.

Q. What is MS Contin?

A. MS Contin is controlled-release form morphine sulfate.

Q. Did there come a time when you proposed that Purdue develop a new controlled-release opioid analgesic?

A. Yes.

Q. Which opioid did you propose?

A. Controlled-release oxycodone.

Q. When did you make that proposal?

A. Very shortly after I first arrived.

Q. And to whom did you make it?

A. Dr. Richard Sackler.

Q. Who was Richard Sackler?

A. He is one of the owners of Purdue.

Q. Why did you propose to develop a new opioid analgesic?

A. To really make up for the deficits that were obvious with MS Contin.

Q. What were the shortcomings of MS Contin that you were aware of?

A. MS Contin, while it controlled pain when dosed every 12 hours in most patients, there remained to be some patients in whom you couldn't provide pain control with every 12-hour dose and you had to dose more frequently.

THE COURT: What year was this when you approached Richard Sackler? You said it was shortly after you --

THE WITNESS: Very shortly after I arrived. It was still '85.

Q. Was this shortcoming, in your view, a result of the morphine itself or the controlled-release nature of the morphine?

A. That aspects of the problem with MS Contin were due to MS Contin and the particular delivery system it was in. It was of

MS Contin rather than morphine itself.

Q. How did you propose to address this shortcoming?

A. The hope was that with the right drug and the right controlled delivery system, we could have levels in blood sustained more than the levels of morphine are sustained with MS Contin dosing. The hope was that with sustaining the levels more, we could have more patients capable of being managed with every 12-hour dosing rather than more frequent dosing.

Q. Were there shortcomings associated with the use of MS Contin related to the morphine itself?

A. Yes.

Q. What were those?

A. Morphine is a difficult drug to use well. To get the dose right, it requires substantial titration, and that had become clear. Titration is not something that a lot of healthcare professionals can take the time to do; and even when they do take the time to do well, it takes time. It is something that clearly needed improving upon, if possible.

Part of the titration process involved side effects. So side effects were a problem clearly with morphine as well, and there was hope that we could improve upon that.

Q. Could you please explain to the Court what you mean when you use the word "titration."

A. Titration is adjusting the dose to one that provides acceptable pain control without unacceptable side effects.

Q. What property of morphine, in your view, led to the need for substantial titration?

A. The low oral bioavailability of oral morphine.

Q. Briefly, what do you mean by "oral bioavailability"?

A. Oral bioavailability is the degree to which a drug becomes available in the bloodstream for interaction with the opiate receptors in the brain and spinal cord after it gets absorbed, after it passes through the liver and gets metabolized.

Q. How did you come to understand these shortcomings of MS Contin?

A. Over a period of years at Memorial dealing with morphine and then later on at Memorial dealing with oral morphine and eventually MS Contin in the context of that experience over that period of time, I became aware of these things.

Q. Why did you propose the controlled-release oxycodone product for development by Purdue?

A. I felt it could improve pain management, that it would be able to address, potentially if not in fact, these problems.

Q. How did you propose that your controlled-release oxycodone product would improve pain management?

A. By really a combination of the attributes of oxycodone, which were unique to oxycodone relative to other opioid analgesics, combined with a delivery system that would present the product in a certain profile in blood.

Q. How many different opioids did you consider before you

settled on oxycodone for development?

A. Between 15 and 20.

Q. What were the properties of oxycodone that led you to select it over the other opioids that you considered?

A. The properties of oxycodone included the fact that there were certain things that we knew about it. It was a known entity to a certain extent. We knew that it was effective when dosed properly. We had reason to believe that it had a high oral bioavailability and a short elimination half-life. Those were among the properties.

Q. What are the benefits of a short elimination half-life?

A. What that really means, it means the drug is turned over fairly rapidly in the body and allows a doctor to determine whether or not the dose he prescribed is the right dose and to change that dose relatively quickly if needed.

Q. You also mention that had oxycodone had high oral bioavailability. Did you consider the relative oral bioavailability of oxycodone compared to morphine?

A. Yes. Yes, I did.

Q. I would like you to look at Plaintiff's Exhibit 1060, which is in volume 3, but we are putting it up on the screen. Is that an exhibit that you prepared?

A. Yes, it is.

Q. Please explain how the two drugs, morphine and oxycodone, compare, in your view.

A. This illustrates two ways in which they differ upon comparison. As I said, morphine, over on the left, has a low oral bioavailability. We see on the axis on the left labeled "Range of Oral Bioavailability." So morphine has relatively low oral bioavailability. Oxycodone, on the other hand, has relatively high oral bioavailability. So that is one aspect in which they differ.

The second aspect, which is a critical one and which is an insight that is absolutely critical to the invention, is that the range around the oral bioavailability of oxycodone had to be narrower than the range around the oral bioavailability of morphine.

Q. What effect, if any, did you believe that these differences in oral bioavailability would have on your controlled-release oxycodone product?

A. I believe that in the right delivery system, controlled-release oxycodone would be able to provide for a narrower range of daily dosages.

Q. Was your belief part of the conventional wisdom in the field at the time?

A. No. No, it wasn't.

Q. Please explain.

A. While we knew that the oral bioavailability of morphine was low and there was good reason to believe that the oral bioavailability of oxycodone was high, I don't think anybody

recognized at the time, certainly my literature searches did not turn it up, that the variability around oxycodone's oral bioavailability would be narrower than the range around morphine's oral bioavailability. I also think that no one thought about how this could result in narrow range of daily dosages.

Q. When did you have this insight with respect to narrower range of oral bioavailability and also narrower ranges of dosages to control pain?

A. By the time I arrived at Purdue, I had that idea.

Q. Did there come a time when you reviewed data that supported your insight?

A. Yes.

Q. What data did you review?

A. I reviewed individual patient daily dosages in patients who had been titrated with MS Contin to a daily dose that controlled pain without unacceptable side effects. These were data that Purdue had generated over a period of years that I had access to, that I began analyzing quantitatively.

Q. Have you prepared an exhibit to help demonstrate your analysis of this data?

A. Yes, I have.

Q. I would like you to look, please, at Plaintiff's Exhibit 1061. Is this the exhibit you prepared?

A. Yes, it is.

Q. Please explain what the data show you with respect to MS Contin.

A. On the x-axis, the bottom axis, we have the dosage, that is, the daily dosage. On the ordinate we have number of patients. The data that I had access to I plotted on this type of graph. What it resulted in is a distribution, frequency histogram, whatever you want to call it, a relationship that is diagrammatically illustrated here in the solid orange line labeled "MS Contin," that line showing the wide, wide range.

(Continued on next page)

Q. What did the data show you with respect to that range?

A. The range was very wide. It quantitated for me what I had as an impression an idea of earlier and really made it clear, clearer, that this is an area that if improved could be a major contribution to pain management.

MR. FILARDI: Objection, your Honor, with regard to foundation of this exhibit. Obviously it's something we can do on cross-examination, but it might be helpful for your Honor to know what it is that's the basis for the creation of this demonstrative evidence. This is supposed to be demonstrative.

THE COURT: I'll let you do it on cross.

MR. FILARDI: Thank you.

MS. LORING: I'm sorry, your Honor. I didn't hear what you said.

THE COURT: He can do it on cross if he wishes, inquire into the basis of the demonstrative.

BY MS. LORING:

Q. Dr. Kaiko, this indicates an 8-fold range for MS Contin. Can you explain how you calculated that range?

A. Yes. I eliminated the extremes, the extreme 10 percent of the patients, so I was left with 90 percent of patients by eliminating the extremes in terms of the daily dose, and then I looked and saw what I had, and what I had wound up with there was an 8-fold range of daily dosages.

Q. What does the exhibit show with respect to controlled-

release oxycodone, or your proposed controlled-release oxycodone product?

A. What this exhibit shows is that the controlled-release oxycodone product would have a different distribution. It would be a narrower distribution. Being narrower, it would have of course a higher peak, and an approximate 4-fold range. And this, graphed here as a dash line, this was an insight I had at this time, given the other things that I knew and the other insight I had. And the bottom line here is that the controlling oxycodone product that he envisioned that I targeted would have an approximate 4-fold range and given dosages required to control pain in about 90 percent of patients.

Q. What was the basis for your reaching this conclusion as to the 4-fold range for controlled-release oxycodone?

A. This was based again on my -- the insight that I talked about earlier, that is, the range in oral bioavailability having to be much narrower for oxycodone, as compared to the wider one for morphine, combined with the other attributes of oxycodone, the effectiveness, the short elimination half-life, and this profile of blood levels that I had in mind.

Q. How did you envision that this narrower rate of dosages required to control pain would affect the titration of THE proposed controlled-release oxycodone product?

A. That it would provide for -- there are all kinds of ways

that one could express it. I chose, as an endpoint, daily dose range, but what leads into that are things like time to stable pain control and ease of titration defined a number of different ways. There are a number of different ways it could express itself.

Q. You stated earlier that shortly after you arrived at Purdue you told Richard Sackler of your idea, your proposal. What is your understanding of what happened after you made your suggestion to Richard Sackler?

A. I recall that Dr. Sackler had thought it was a good idea and he went about progressing that program.

Q. Did there come a time when you discussed your idea for a controlled-release oxycodone product with others at Purdue?

A. Yes.

Q. What were the circumstances of these discussions?

A. Those discussions were part of the routine -- I guess they were monthly at that point -- R&D meetings.

Q. Who attended these meetings?

A. Ben Oshlack, oftentimes other people from this formulations group. I always attended those. Paul Goldenheim always attended those. Richard Sackler sometimes attended those Eventually Mark Chasin attended those. Other people in non-clinical research, as well as clinical research, participated in those meetings as well.

Q. Who was Ben Oshlack?

A. Ben Oshlack has led up the formulations group for a long time now.

Q. And who was Paul Goldenheim?

A. At that time Paul Goldenheim was a medical director.

Q. What did you say about your idea for a controlled-release oxycodone product?

A. What I tried to express very early on was that what I had in mind was a product that would have a certain profile of blood plasma concentrations over time, and what I was looking for and which I expressed early on is I wanted something with an early peak, with a peaky kind of initial profile of blood levels, rather than a flat curve. But I wanted these sustained. I wanted these sustained but yet being peaky early on.

Q. Was there any discussion about how to achieve the blood level profile that you envisioned for the product?

A. Yes. There was discussion early on about starting by matching the initial portion of the dissolution curve for MS Contin, trying to match the initial portion of the dissolution curve for MS Contin with the controlled-release oxycodone test formulations.

Q. What does the term "dissolution profile" mean?

A. "Dissolution profile" is an in vitro test that formulators often use early on in the development programs of test formulations, experimental formulations of controlled-release

products. It's a benchtop way of looking at how the tablet produces drug over time in vitro.

Q. What was your understanding of why there was a decision made to try to match the early portion of MS Contin as a dissolution profile?

A. MS Contin had an early -- was early -- was peaky early on, and that part of the MS Contin averaged -- I mean, there was a lot of variability in blood levels, but it was clear that it had an early rise in blood levels. And that part of MS Contin I wanted to keep. I thought that the way to start, with an experimental Oxy -- controlled-release oxycodone formulation was to start with an experimental tablet that would match the initial portion of the dissolution curve. It made more sense than starting anywhere else.

Q. What happened after you explained your idea to others at Purdue?

A. Well, they were well accepted, and the first move and the move that made sense was that of the formulators, and they went and began formulating experimental controlled-release oxycodone tablets.

Q. Were you apprised of the formulators' progress in this regard?

A. Excuse me?

Q. Were you apprised of the progress of the formulators?

A. Yes.

Q. Did there come a time when you began clinical testing of controlled-release oxycodone formulations?

A. Yes.

Q. When was that?

A. That was in 1987.

Q. What involvement if any did you have in the selection of formulations to be used in clinical studies?

A. I participated in the choice of experimental formulations for that initial study.

Q. I would like to talk now about the types of clinical studies that you've been involved with during the development of OxyContin and other drugs. Have you prepared a demonstrative exhibit describing --

A. Yes, I have, yes.

Q. -- the different categories of clinical study?

A. Yes.

Q. I'll show you Plaintiff's Exhibit 1062, which is actually a board. It's also in volume 3 of the exhibit books.

A. Thank you.

Q. Is this the board you prepared, Dr. Kaiko?

A. Yes, it is.

Q. What is the first type of study depicted on the board?

A. The first type of study is a single-dose study which is designed primarily to look at blood levels.

Q. What types of patients are these studies conducted in?

A. Yes.

Q. Have you prepared demonstrative exhibits to demonstrate the source of some of the language from the '912 patent?

A. Yes.

Q. I would like you to look, please, at Plaintiff's exhibits 1065 and 1066. These are demonstratives that are in volume 3 of your book. Can you explain, please, to the Court what the highlighting is that's in both of these documents.

A. The highlighting in these documents show the text from my invention disclosure that is taken verbatim and incorporated into the written patent.

Q. And there are also some numbers in the margin. Will you please explain the significance of the numbers.

A. Yes. If one looks at the invention disclosure at the highlighted areas, each paragraph in that document is numbered. If you go over, then, to the '912 patent, those highlighted areas that are taken from the invention disclosure have the same number in them corresponding to the invention disclosure.

So while major sections of the invention disclosure are in the patent -- not in the exact same order, but we've noted them and coded them so that you can see where in fact they appear.

Q. Let's look back at the exhibit, the patent, which is Plaintiff's Exhibit 8. And I'm going to put on the screen column 1. I would like you to focus on lines 9 through 17.

There's a reference there to "surveys of daily dosages," "required to control pain." Do you see that?

A. Yes, I do.

Q. To what does that refer?

A. That refers to the survey that I described yesterday where I examined individual patient MS Contin daily dose requirements to control pain from a series of separate studies and over a period of a couple, few years, and plotted out on a distribution or frequency histogram graph the number of patients that required various doses.

Q. Turn now, please, to column 3. I would like you to focus on lines 33 through 40. The paragraph starts "it has now been surprisingly discovered." To what does this paragraph refer?

A. This paragraph again refers to my insight that a reduced range of daily dosages were required in a majority of patients as compared to twice the range with the prototype analgesic for these kinds of patients.

Q. Which is?

A. MS Contin.

Q. What if anything does this statement say about whether you had proved this four-fold range through clinical studies?

A. Nothing, in terms of scientific proof.

Q. At the time that the '912 patent application was filed, did you have any scientific proof that there was a reduced range with OxyContin?

A. No.

Q. Then what was the basis for this statement?

A. It was based on the insights I had, combining those insights, and knowing that in the context of a certain type of controlled-release profile, with oxycodone this had to be the case.

Q. At the time that the application for the '912 patent was filed, did you believe that this statement was true?

A. Yes.

Q. Do you believe it today?

A. Yes.

Q. I would like you to look now at column 5 of the patent. There's a paragraph that starts at about line 5. First I would like you to focus on lines 5 to 9 and tell me what's discussed there.

A. What's discussed there is the fact that, at the time, in this area of controlled-release dosage forms, that provide for the 12 hours' effect, the idea that most people had was to produce that steady state of a flat, essentially a flat curve, that that was the goal. And a flat curve typically has its maximum concentration at between four and eight hours. Whereas --

Q. Let's --

A. Right.

Q. Let's look now at the next piece of that paragraph, lines 9

blood levels are more consistent. In addition to that, what this is saying is that if a doctor chooses a certain dose of OxyContin or doubles a dose of OxyContin in a particular patient, the doctor could be much more confident, five times more confident, in knowing what the concentration of drug is going to be, as compared to if he was using MS Contin.

Q. Are these conclusions consistent or inconsistent with your insight as to the narrower dosage range for your CR oxycodone invention over CR morphine?

A. It is consistent. It is a clear reflection of the invention.

Q. Now I would like you to look at the third full paragraph under "Conclusions," and the second sentence, which says, "The median time to achieve stable pain control was two days with both treatments, and the number of dose adjustments required and rescue medication use were similar for both drugs."

How does this statement affect your belief or your insight into the reduced range of dosages needed with your controlled-release oxycodone invention?

A. This statement does not alter my insight.

Q. Can you explain that, please.

A. Yes. Again, this study was designed with a different purpose in mind, and it was well controlled for that purpose. That purpose was determining parameters related to blood levels and their fluctuation. The study was not designed to look at

this outcome of these ease of titration. It didn't have validated methods or procedures, it didn't have the appropriate treatment controls. The number of subjects were also not chosen on the basis of this kind of outcome.

Those in the area of analgesiology would know by the design of this study that that would be the case, and that what we are just looking at here is a characterization of what is happening with these patients before the true experiment is being done.

Q. I would like you to turn now to P187369, under the heading "Study Population." Tell us how many patients participated in this study.

A. I'm sorry. Which page?

Q. It is P187369. I believe the information is in the second paragraph under the heading "Study Population."

A. There were about 50 patients in each of the two treatment groups.

Q. Did you believe that about a hundred patients were sufficient to test ease of titration?

A. No.

Q. Again, how many patients would be needed?

A. I would estimate, without going through the calculations, that hundreds to thousands of patients would be required.

Q. Were you aware of these two studies, the Kalso and Mucci-LoRusso studies during at least some of the applications

that led to the patents in suit?

A. Yes.

Q. Are you aware that inventors have a duty to tell the patent office about any information that they know of that is inconsistent with statements they make about their invention?

A. Yes.

Q. Did you tell the patent office about these studies?

A. No.

Q. Why not?

A. They didn't either prove or disprove the invention. In fact, the results from both these studies were quite consistent with my insights and the invention. The purposes for which these studies were designed, the results of these studies demonstrate, were fulfilled and quite consistent with the invention. There was nothing inconsistent to bring to anybody's attention.

Q. Dr. Kaiko, did you intend to deceive the patent office when you told them about your reduced range of daily dosages with your controlled-release oxycodone invention?

A. No.

MS. LORING: I have no further questions, your Honor.

THE COURT: Thank you. Let's take a ten-minute break.

(Recess)

THE COURT: Dr. Kaiko, before we begin cross-examination, you said that, if I understood you

correctly, to test ease of titration, either of these two studies that we have been talking about, the Kalso study and the other one, would require hundreds, even thousands, of participants, is that right?

THE WITNESS: That would be my estimate without going through the calculations, yes.

THE COURT: If the study group for each of them consisted of hundreds or thousands, could ease of titration be gathered from the studies as conducted? In other words, is the only thing lacking the proper number of subjects?

THE WITNESS: No. There are two other things that are lacking. One are control treatments. One will want to have a treatment that on one extreme and another treatment on the other extreme, two different treatments that the medical community agree have different ease of titration.

The ability of the study to demonstrate that there is a difference in titratability between that negative standard and that positive standard would be a measure of the sensitivity of the study. Once having established that, then you could look at the two items of interest within the study, which is ease of titration with MS Contin and OxyContin, and make statements as to whether or not the study was sensitive enough to determine whether or not differences existed.

So in addition to the numbers of the patients, a second issue is control treatments.

Contin with experimental formulations of controlled-release oxycodone.

Q. Have you ever used the term, you wanted the formulators to mimic the dissolution profile of MS Contin?

A. That sounds familiar.

Q. Is this something that derives from you? You said you were the -- I don't recall your exact words but you said that you were basically the driving force, the initiator of the whole project for what eventually became OxyContin; isn't that correct?

A. That's correct.

Q. And my question to you is, do you recall in that context whether you were the first to say, at Purdue, to the formulators, people like Ben Oshlack and John Minogue, let's match the dissolution profile of MS Contin?

A. I recall first saying that my interest was to get a certain profile of blood levels that would result in a certain clinical outcome. And then there was discussion of how we might, or where we might start in order to achieve that end. And there was discussion amongst us -- I don't know who first mentioned it, but we talked about matching the profile, and it was suggested that the place to start might be matching part of the profile of MS Contin.

I matched on to the -- I, to me, my interest was, yes, it's a reasonable place to start, but to me it's most important

that you match that initial part of the curve, because I was interested in getting something that had certain things in characteris -- in common with MS Contin that were things that happened early on. But I didn't want to -- I didn't want to match the complete blood level profile among other things with MS Contin.

Q. Well, I'm speaking of the in vitro dissolution profile of MS Contin.

A. Yes. We agreed that that would be a place to start. I'm not sure I was the first one to talk about matching, but when it was brought up, I said, let's match -- you know, I was interested in matching that. And we agreed that that made sense. That made sense.

Q. Do you know if any work was done on that, if matching, mimicking the in vitro dissolution of MS Contin was done before you arrived, in 1985, September of 1985, at Purdue?

A. I hadn't become aware of that until litigation.

Q. But you're aware of it now?

A. Yes.

Q. But whatever, let's not get bogged down in -- whatever the starting point was, is my understanding correct that the purpose at Purdue, yourself and Ben Oshlack and other people, the purpose of mimicking the profile was to cut down the number of iterations, the formulation, reformulation process, the number of iterations to arrive at a workable formulation? Is

that correct?

A. Yes.

Q. And would I be correct in stating that in this case, with regard to oxycodone, there were no iterations; isn't that correct?

A. There were iterations in terms of the formulation certainly. Whether or not there were iterations in terms of the matching the initial part of the profile, I mean, I think they made a number of different experimental formulations within a period of time.

Q. Sir, isn't it true that with regard to the development of OxyContin, that is, Acrocontin oxycodone, it was not an iterative process; it was not a trial-and-error process; Purdue was lucky because you hit it on the first trial? Purdue was very lucky and you hit it on the first trial. Isn't that correct?

A. Purdue was lucky in the thought --

Q. Isn't that correct, sir?

A. In the term --

Q. Is that correct, sir?

A. Not as stated. It's vague as stated and I'd like to say that it's correct to the extent that the first formulation brought in demand.

Q. Purdue, and it's been your testimony, Purdue has been very lucky in this case because there was no iterative process in

the development of Acrocontin oxycodone or OxyContin; isn't that correct?

A. That's correct.

Q. You arrived at Purdue in September of 1985. I think you signed your employment agreement September 30, 1985. Lawyers get to know that stuff on cases like this. But is that your recollection?

A. Yes.

Q. And would I be also correct in stating that it is your position, Dr. Kaiko, that you are the originator, you are the driving force, you are the source and start of the project to develop at Purdue controlled-release oxycodone?

A. Yes.

Q. Now, when you arrived at Purdue in 1985, did you in any way attempt to familiarize yourself with the prior work of Ben Oshlack and his colleagues at Purdue?

A. No.

Q. So you only realized today that in fact Oshlack and his coworkers had already started, for example, to mimic MS Contin, its profile, before you came to Purdue; isn't that correct?

A. No. I have no reason to believe that they ever tried to mimic MS Contin before I arrived at Purdue.

Q. So you haven't been shown any documents in this case that were written by Ben Oshlack with regard to MS Contin and mimicking its in vitro profile before the time you came?

A. I don't recall seeing it.

Q. And you're aware that Mr. Oshlack will be called on behalf of your company, Purdue, to testify as the next witness in this case; are you aware of that?

A. Yes.

Q. He would be a good source to know what he did prior to the time you came; wouldn't that be correct?

A. Yes.

Q. But whatever you did, I think I understand from your testimony today that your contribution to the invention had to do with the plasma oxycodone concentrations and times and the reduction of the dosage range. And that is, in other words, quicker titration time. Is that correct?

A. And the rest of the clinical related information in the patents.

Q. Right. By the way, how did you prove -- well, I think you testified to this. Prior to the filing of your application in 1992, you really had no proof, scientific proof, of any nature, as to reduction in range, ease of titration; that's correct, isn't it?

A. Yes.

Q. Now, you just mentioned, when I asked you your involvement, you said "and in addition the clinical aspect of this." And that's the purpose of your original chart, Plaintiff's Exhibit 1064, which I have modified to be Defendant's Exhibit 4384.

Q. Now we're back in the September 28th memorandum that you wrote. See it here. It's Defendant's Exhibit 3629. And on the second page, you write, and your counsel focused in on a few other paragraphs which I won't focus in on, but I would like to focus in on a paragraph that your counsel didn't focus in on, and that is the one that says, "I attach a copy of a draft analysis." And that analysis is attached to Defendant's Exhibit 3629. Do you see what it says there? "I attach a copy of a draft analysis plan for OC93-1001 in which Dr. Fitzmartin, Mr. Thomas, Mr. Komorowski and I attempted to deal with these issues; this is not meant to be either complete nor sufficient (let's be positively creative)." Do you see that?

A. Yes.

Q. Would I understand that at this point in time you are in fact taking the lead in attempting to prove the primary claim of ease of titration; isn't that so?

A. No, I wouldn't say that. What I was taking the lead in is reviewing data from studies that were already completed or planned for other purposes, designed to answer questions other than this question, and seeing what we could find in fact in those studies that was related to the invention, to see, in addition to what the study was designed to do that was consistent with the invention, such as the fluctuation and variability in study 1001, but I never believed that I could prove reduction in daily dose range on the basis of going back

to these studies designed for other purposes.

Q. Let's go on to Defendant's Exhibit 3739. Now just stay there one moment here. 3739 has on its face the distribution list and all the people. Is this generally the people who were on the distribution list for the OxyContin project, like yourself, Innaurato, Goldenheim, Grandy, Chasin, Oshlack?

A. Those names you mentioned were among those who were usually involved, yes.

Q. And what we see here, though, is a mean entity if you will, a different entity, a non-personal entity. There's the IND/NDA file. Do you see that?

A. Yes.

Q. Were you familiar with that file at the time?

A. No.

Q. Have any reason why all of this, these internal memos, are being sent to that file?

A. No.

Q. Can we go on to the next page, please. Here is Dr. Reder, OxyContin project team. You were on that team, right? And this is May 3, 1994. And what they're talking about is a preliminary report on the OxyContin tablets investigator survey. OxyContin tablets, that's oral dose, right?

A. Yes.

Q. And OxyContin is your invention; isn't that correct?

A. Yes.

Q. And at least at this time it appears that you are the leading promoter of the primary claim, ease of titration. Doesn't that appear to be the case to you from these documents?

A. That appears to be the case, yes.

Q. And what does Dr. Reder report, at least preliminarily at this time, May 3, 1994? "OxyContin benefits included the following: Easier titration than Duragesic (but not MS Contin or oxycodone IR)"? Do you see that? And it's the first on the benefit list. Do you see that?

A. Yes.

Q. Duragesic is the fentanyl patch?

A. Yes.

Q. Not an oral product?

A. No.

Q. So you had a benefit of ease of titration over a non-oral product, correct?

Correct? According to this report. There's an easier titration than the Duragesic fentanyl patch.

A. Yes.

Q. But not the oral products, like MS Contin. Correct?

A. That's what it says.

Q. OK. How about oxycodone? Is that an oral product?

A. Yes.

Q. Now, let's go to the '331 patent application.

A. Could I just complete my answer for a moment?

Q. Answer to what?

A. The question. That's what it says there, but you have to appreciate, these are 11 doctors who have very limited experience with OxyContin. It's a documented anecdote of a very small number of people.

Q. So at least at this point in time you were very much interested in proving the primary claim, and the preliminary indication was against the primary claim, but you believe that the indication wasn't important because of the small number of doctors who were surveyed?

A. This is -- this opinion of 11 doctors with limited experience with OxyContin, it doesn't prove or disprove anything. It's not -- when I saw this memo, you know, frankly I had to chuckle to a certain extent, because this is not a way -- this type of survey is not a way of answering a question.

Q. OK. But you know this document pretty well, don't you, because if we go to the second page -- let's go to the second page of this document. And let's go down to the fifth paragraph down, maybe the first three or four lines, please, Molly.

You know this well enough to know exactly the number of doctors that were surveyed, and you probably know it well enough to know that 0 out of 11 felt it was easier to titrate than MS Contin, and 1 out of 11 felt it was easier to titrate

than oxycodone IR tablets.

MR. FILARDI: No, it's the first three lines. OK.

Q. I'm sorry to be distracting you with that, but you see that, right? This is 0 out of 11?

A. I see what that is. And this is not science.

Q. And this is 1994, right?

A. Yes.

Q. So if we can gather up whatever we've learned at this point, 1994 in time, you've already filed your patent application on the invention in November of 1992, correct?

A. Yes.

Q. And based upon your intuitive knowledge at the time, you said that -- whatever you said about the invention, that part of the investigation was a reduction in range, ease of titration, correct?

A. Part of the invention was reduction to range, reduction in range.

Q. OK. We'll go back and see the exact language that you used in the course of time. But I want to just get fixed in our minds that as of '94, you were attempting to prove the primary claim. You thought it was imperative, but your early indications were that it may not be true. Fair?

A. No. Unfair. Wrong. Where we designed studies to look at tendencies of the invention, we found data consistently consistent with the invention.

Q. Did that occur, start any time prior to 1997?

A. Yes.

Q. And were those data, were those reports submitted to the FDA?

A. They were consistent with the invention.

Q. Were those reports that were consistent with the invention that is surprisingly found and proven for OxyContin over MS Contin, were they submitted to the FDA?

A. That -- I think most of what we -- much of what we did was submitted to the FDA. We don't --

Q. And if it was submitted to the FDA --

A. There are some things that we don't submit to the FDA.

Q. I'm sorry. Are you finished, sir? Forgive me. I interrupted you.

A. Yes. Yes.

Q. I apologize. OK. My point is, to the extent these documents exist, would they be in the files of Purdue?

A. I don't know that they all would be.

Q. Where would they be, if not in the files of Purdue?

A. Not everything we did we saved.

Q. OK. So some things have been destroyed.

A. Most likely.

Q. OK. Now, of this portion of the documents which support the primary claim that survived destruction, do you know whether those documents, from the files of Purdue, were sent to

the FDA?

A. I know that some were.

Q. And do you know of any reason why those documents have not surfaced in this case?

A. They have surfaced in this case.

Q. And your counsel will point them out if they exist. Do you think that's a reasonable assumption, prediction, what might happen on redirect examination?

A. I don't know, sir.

Q. OK. Now, let me ask you this. Were any of those materials that supported -- demonstrated that the primary claim was true, were they submitted to the U.S. Patent Office at any time?

A. What we had observed was not --

Q. No, I'm not asking about "observed." I want to know about the studies that you did or the evidence that you had that supported the primary claim ease of titration. Were they submitted, in any form -- oral, written -- to the U.S. Patent Office?

A. No.

Q. Let's go back to the '331 patent. I would like to get that up. I think it's 2044. Now, you are not an inventor on this patent, but during the course of prosecution in this case, do you recall that the claims of Oshlack and his co-inventors were rejected in view of the '598 patent and the '341 patent?

A. Yes.

of direct.

MR. FILARDI: Could we get Defendant's Exhibit 2049, the patent. Specifically, column 5, lines 5 to 15.

Q. I would like to parse through this paragraph a little bit. Your counsel directed you, I believe, to the second part of this, but I would like to take the whole paragraph.

"In order to obtain a controlled-release drug dosage form having at least a 12 hour therapeutic effect, it is usual in the pharmaceutical art to produce a formulation that gives a peak plasma level of the drug between about 4-8 hours after administration (in a single dose study)."

Do you see that?

A. Yes.

Q. Were you aware at that time that there were several drugs, formulations, controlled-release drug dosage formulations for moderate to strong opioid analgesics that in fact achieved a peak plasma level of between 2 to 4 hours for a 12-hour drug prior to the time this statement was made by you and your colleagues, co-inventors, in November of 1992?

A. Other than MS Contin, I was aware of another 12-hour release morphine product that was being characterized as having an ideal pharmacokinetic profile for 12-hourly oral controlled-release opioid for moderate to severe pain --

Q. Let's see if we can take this --

MS. LORING: Your Honor, he hasn't completed his

answer.

A. -- and that had a Tmax that was between 4 and 8 hours. I think the only other one I was familiar with was the twice-a-day hydromorphone product that is in that category of drugs that you had made reference to. So that is what I was aware of at the time.

Q. Did you have a hand in writing or giving input to the writing of this particular representation to the patent office and communicating to the patent office that it is usual in the pharmaceutical art prior to your invention that to produce a formulation that gives you a 12-hour drug, you've got to have a peak plasma level of drug between 4 and 8 hours? Was that you who gave that information to the patent lawyers?

A. When I received the draft patent, I discussed various portions of it with outside patent counsel, and changes were made, including changes in this section. I recall how people felt about the early peak that MS Contin had. I knew what the conventional wisdom was at the time regarding the desire, the goal of the flattest curve possible for controlled-release drug for moderate to severe pain. And I revised this. I had input to this. Parts I agreed with, parts I didn't, and it reflects my position as it is written today.

Q. This is my question. Doesn't that communicate to the patent office that for a twice-a-day drug, twice-a-day daily drugs --

A. Yes.

Q. -- in other words, at least 12-hour therapeutic effect, that in the past there was a 4- to 8-hour peak level for plasma and that was usual, isn't that correct? Isn't that what you are communicating in the application?

A. In the art, the goal, the conventional wisdom within the art was to produce a flat curve with a peak in the mid range of that curve. The products that I had been aware of included products that met that goal, and that is what people considered the appropriate product for the art to develop.

Q. That was something in the 4- to 8-hour range, isn't that correct?

A. Yes.

Q. Is it not a fact that as of the time of the filing of this application for the '912 patent and the other patents in suit, you were in fact aware that CR morphine, controlled-release morphine, in fact had a 2- to 4-hour Tmax, and that was for MS Contin, isn't that correct?

A. Yes.

Q. You in fact coauthored an article in 1986 showing that MS morphine had a 2 to 4 to give a 12-hour twice-a-day drug, isn't that correct?

A. Yes.

Q. Would it have been fair to point that out to the examiner at this time, that the closest commercial piece of prior art,

MS Contin, against which you did a lot of studies and comparisons, had the same profile: It was 2 to 4 and gave a 12-hour twice-a-day drug?

A. I disagree. We were very disappointed in MS Contin not having the sufficient data to support a 12-hour duration claim alone, that the drug couldn't perform in most all patients when dosed appropriately every 12 hours, requiring that some patients be dosed much more frequently.

Q. That is not what you wrote in 1986, is it? It is not what you wrote when your company was promoting MS Contin, was it?

A. We promoted that the majority of patients can have their pain controlled with every 12 hour dosing with MS Contin, and that is the truth and that is not inconsistent with what I just said.

Q. But you described it in your publication -- could we have DX2766 -- as a 2 to 4 rather than an 8, isn't that correct?

A. Oh, yes.

THE COURT: For Tmax?

Q. For Tmax?

A. Yes.

Q. I don't think we need that then.

Let's go on to the controlled-release codeine. Isn't it a fact that you knew Tmax was 2 to 4 for controlled-release codeine as early as 1988, several years before the 1992 representation in your patent? Isn't that correct?

A. MS Contin is --

Q. I am not talking about MS Contin. I am talking about CR codeine, controlled-release codeine.

A. That is not appropriate for moderate to severe pain.

Q. I'm sorry. Forgive me. I missed what you said. It is not appropriate for?

A. I don't think that falls within the group of drugs where you first asked the question and characterized them as drugs for moderate to severe pain. That does not fall within those.

Q. Let's take a look at what you wrote in your patent application.

MR. FILARDI: Can we go back to the patent application, please, column 5, 5 to 15. DX-2049, column 5, lines 5 to 15.

Q. Here you don't make a distinction based upon level of pain, do you. You say, in order to obtain a controlled-release drug dosage form having a 12 hour, it is usual in the pharmaceutical art to produce a formulation that gives a peak plasma level, Tmax, of 4 to 8 after administration. It says nothing about moderate to strong pain or anything like that.

A. Elsewhere in the specifications I make it clear that we are talking about drugs for moderate to severe pain, and I list several candidates, and codeine is not among them.

Q. Certainly not in this paragraph with regard to that representation, isn't that correct?

A. That's correct.

Q. But you knew more at that time in November of 1992, because you knew that controlled-release hydromorphone --

MR. FILARDI: Could we get Defendant's Exhibit 3282, please, at page 309298.

Q. Here is a final clinical report, correct, that you signed, which shows this drug, controlled-release hydromorphone, as having a Tmax between 2 to 4, isn't that correct? You knew about that?

A. Yes.

Q. You knew that in 1988, isn't that correct? 1988. Yes, I represent to you it is 1988. And you knew more than that. You knew with regard to controlled-release dihydrocodeine of the '984 patent, that it in fact was another drug that had a Tmax of 2 to 4, well prior to your patent disclosure, isn't that correct?

A. Another drug for more moderate pain, a drug I hadn't had any clinical experience with in terms of these studies, wasn't in my mind as I was thinking about this.

Q. But, Dr. Kaiko, you were filing an application claiming a controlled-release opioid for oxycodone, right?

A. Yes.

Q. Didn't you look back into the prior art disclosures with regard to the same type of formulations, controlled-release opioid analgesic formulations? That is right into the area of

the subject matter of this patent. You didn't think to mention that to the patent office?

A. I was familiar with most all of these formulations.

Q. Did you tell your lawyers?

A. My lawyers appreciated this as well.

THE COURT: Is this an appropriate time to end, sir?

MR. FILARDI: It is, your Honor.

THE COURT: Why don't we break now. We will pick it up tomorrow at 11:00 a.m. Thank you.

(Adjourned to June 4, 2003, at 11:00 a.m.)

phone.

What about the alternative?

MR. SCHWARTZ: Video link.

THE COURT: A video feed that can be -- I know at 40 Foley Square they have the facilities for that. I don't know at the other end; that may be the issue.

MR. SCHWARTZ: That's what I would suggest, your Honor, that we do it with a video feed. I've heard of that being done before and I've been involved in it myself.

THE COURT: Since you are asking to have me review the video, it's not as if I were reading the transcript and can do it in a shorter period of time. Since it is in real time, it would take the exact same time for me to view it as it would for you to take it. Thinking it through, then there's a problem, because the reason I'm not having trial on Friday is because I have other cases.

MR. SCHWARTZ: If we had a video feed we could it in regular trial time any day, Wednesday, Thursday.

THE COURT: Yes, but doing it at a time when I could otherwise see you, short as the trial, from the standpoint of the last day of trial. In other words, I can watch it on a Saturday or Sunday.

Work it out, and if you want to do it on a video feed, we'll just have to arrange it at a time when I can be watching.

And I guess the video feed only has to be one way.

That may make it easier. I need an audio feed the other way, but I just need a video feed to me.

See if you can work it out.

MR. SCHWARTZ: OK. We'll try.

THE COURT: All right. Proceed.

MR. FILARDI: All right. Thank you.

CROSS EXAMINATION

BY MR. FILARDI:

Q. Good morning, Dr. Kaiko.

A. Good morning.

Q. Let me see if we can pick up where we left off yesterday.

MR. FILARDI: Can you get on the screen the '912 patent, Defendant's Exhibit 0249, particularly the column, the language that we were discussing in column 5, line 5.

Q. Do you recall our focus toward the end of the day, yesterday, was on the, if you will, the T max and the prior art at 4 to 8, whereas with the invention it was 2 to 4. Do you recall that?

A. Yes.

Q. And if I recall your testimony --

A. Oh, I'm sorry, no. It's 2 to 4 1/2, sir.

Q. OK. When you say 2 to 4 1/2, there would be some overlap actually between what you found and in the prior art, because within the 4.5, 4 1/2 hours and 4, there was an overlap with the prior art. Isn't that correct?

A. Yes.
Q. And that 4 1/2 appears in claims, doesn't it?
A. Yes.
Q. And that portion is actually a capturing of the prior art, at least in that portion of the claim; isn't that correct?
A. I can see how you can say that to some extent.
Q. Now, yesterday, if I recall correctly, you testified that as of the time of filing, writing this paragraph to the patent office, you were aware that there were several controlled-release opioid analgesic formulations that actually were characterized by a T max of 2 to 4; isn't that correct?
A. Yes.
Q. And those included controlled-release codeine. Do you recall that?
A. Yes.
Q. And you were aware of that at the time. And it also included controlled-release hydromorphone; isn't that correct?
A. Yes.
Q. And controlled-release dihydrocodeine, the 984 patent. Isn't that correct?
A. Yes.
Q. And then also controlled-release morphine, the MS Contin, you were aware that that had a T max of 2 to 4 in the prior art; isn't that correct?
A. Yes.

Q. And significantly, the 2 to 4 of the morphine was contained in quite a bit of literature, the description of it, quite a bit of literature of the Purdue Company, your company, isn't that correct, prior to November of 1992? Isn't that correct?
A. Yes.
Q. I would like to show you an exhibit that has been marked as Defendant's Exhibit 3260. I believe it's in the book that is in front of you, but I will get it up on the screen. Maybe you are familiar with this. Are you familiar with literature like this, where MS Contin was promoted?
A. Yes.
Q. And if you were to turn to the second page of Defendant's Exhibit 3260, you would see that it's promoted as a 12-hour drug; isn't that correct? Prominently promoted as a 12-hour drug.
MR. FILARDI: It would be down at the bottom of the page.
Q. Isn't that correct?
A. It was promoted primarily as a 12-hour drug, yes.
Q. And this brochure is well prior to November of 1992, isn't it, sir?
A. Yes.
Q. This is roughly a mid 1980's brochure; is that not correct?
A. Yes. Also in here is acknowledgement that it's also indicated for every 8-hour dosing.

Q. So it's indicated for both 12 hours and 8 hours depending upon how you administer it?
A. No. It depends on whether or not the patient can be controlled every 12 hours or not.
Q. Let's go to the next page. It has P-041767 down at the bottom. Do you see that page?
A. Yes.
Q. And that would indicate clearly that MS Contin has a T max of 2.7. Isn't that correct?
A. Yes.
Q. What is Roxanol SR tablets?
A. That is a controlled-release oral morphine formulation that differs somewhat from MS Contin.
Q. That also has, that drug also has a T max of between 2 and 4 hours; isn't that correct?
A. Yes, but its efficacy dynamics are quite different.
Q. It falls within the general purview of an opioid analgesic in the prior art controlled-release formulation?
A. In a general sense, but it's not as potent, and its onset of analgesia is significantly different from that of MS Contin.
Q. You also mentioned yesterday during the course of your testimony that one of your contributions is to focus in on early peak T max for oxycodone?
A. I wanted to have an early peaky profile, yes.
Q. Can you turn to page 041769, take a look at what in the mid

1980's your company was showing as the curve for the MS Contin tablet. Wouldn't you say that's pretty peaky?

A. Yes.

Q. Tell me about this MEAC, the minimally effective analgesic concentration. Would I be correct that this graph indicates, to anyone who sees it, anyone who reads it at the time, that roughly the MEAC, the minimally effective analgesic concentration, for MS Contin was approaching, was a little less than 15. Can we call that 14?

A. I wouldn't say that, no.

Q. And what would you say? What does this graph tell you about the MEAC?

A. It's in the context of the whole document such as the previous page. It's laid out there that MEAC was arrived at, and what illustrates it are the results from eight different studies utilizing variously different ways of getting in testament of MEAC and winding up with a threefold difference from about 6 to about 20 nanograms per ML.

So to say that the MEAC is 14, I think, is mischaracterization of the MEAC in the context of the whole document.

Q. In the context of this entire document, in the mid 1980's, did you, sir, have an understanding that oxycodone at that point in time was about twice as potent as MS Contin?

A. Yes.

asking to have any idea of whether that might be generally high, low, or right. Nor do I have the statistical skills to calculate the power of the study.

Q. Would you please now turn your attention to Defendant's Exhibit 4355. By the way, this -- I'll just, I'll continue.

4355, here again it's another portion of the Kalso study. Is that correct?

A. Yes.

Q. Submitted to the FDA. Correct?

A. I don't know.

Q. I see on the second page there's your name but there's no signature. Do you recall whether in fact this document was signed and submitted to the FDA?

A. I don't know.

Q. Look at the first page of the document, 642906. Do the dates there generally indicate -- are they accurate to your recollection as the start date, the end date, and the study report date? And I'll read those dates and ask you whether they are consistent with your recollection of the timing of the Kalso report submitted to the FDA. Start date February 22, 1994; end date May 16, 1995; study report date July 29, 1996. Correct?

A. Maybe you misspoke or I misunderstood you, but the report date didn't start and end under those dates. They're the study dates. Those are the study dates, the time that the first

patient was dosed and the last patient was dosed.

Q. OK. Thank you very much. This is work that was sponsored by your company, Purdue?

A. Yes.

Q. And Purdue selected the investigator, Kalso?

A. Yes.

Q. For the study. And did your company receive regular reports as to the progress of the study as it proceeded?

A. Yes.

Q. Could you please turn to page 642954. Would I be correct in stating that that page identifies as a primary efficacy variable of the study, quote, time to achieve stable pain management, end quote?

A. Yes. But that doesn't say the study was designed to determine whether or not there's a difference between treatments in that regard, as I had probably said to you many times already.

Q. Are you finished, sir?

A. Yes.

Q. OK. Could you please now turn to page 642793. Under the heading "time to achieve stable dosing," would you turn to the last sentence. It says, "The median time to stable dosing was three days for CR oxycodone and 1.5 days for CR morphine. There was no significant difference in the time to achieve stable pain control." My question is, were you aware of that

statement as of August 18, 1996?
A. Yes.
Q. Did you make any recommendation to your patent counsel in connection with then pending applications for the patent in suit that that information be disclosed to the patent office?
A. No.
Q. Could you go to the next page. I'm sorry. It's not the next page. It's the page that bears production number 642994, page 89 of this exhibit number Defendant's 4355. Do you see this is the conclusions page; is that correct?
A. I'm sorry. What page are you on again?
Q. 642994.
A. Yes.
Q. Under the heading 8.2, the conclusions are reached as to the efficacy of OxyContin versus MS morphine. Is that correct?
A. Yes.
Q. And in there, the third line down, and I read to you, and it reads, quote, In the titration period there were no significant differences between CR oxycodone and CR morphine treatment groups with respect to the number of days required to achieve stable pain control. Did I read that correctly?
A. Yes.
Q. And as of this time, August 16, 1996, you were aware of that conclusion being reached?
A. Yes. But that's in the context of study, where a

knowledgeable reader will recognize a study is not designed to determine whether that's the case or not. A study is not determined to prove or disprove that. What the study was in fact designed to do, it obtained information that was consistent with the patent.

Q. And this information was given to the FDA?

A. Yes.

Q. And this information was not given to the patent office?

A. Correct.

Q. I turn your attention now to Defendant's Exhibit 4359 -- we've already done that. Can we jump over to 4371.

MR. FILARDI: Your Honor, this is my last exhibit. I know it's ten after 1. Would you like me to conclude? I can conclude.

THE COURT: I would like you to finish -- if you're able to finish the cross, then I think you should --

MR. FILARDI: I'm going to --

THE COURT: -- take the time you need, and when you're done, cross will be finished.

Q. Defendant's Exhibit 4371. Do you know what this document is?

A. This looks like a document to a regulatory body other than the FDA. Which regulatory body that -- a non-U.S. regulatory body other than the FDA, other than one in the U.S.A. But I don't know what country it is.

Q. And this was submitted to whatever body it was submitted to in 1996?

A. There's a June 16, 1997 date on the lower bottom of the page I'm looking at.

Q. I'm sorry. June 1997. Correct. I agree. And was it submitted on or about that time?

A. I don't know when it was submitted. I'm reading the dates off a piece of paper.

Q. Could you turn now to the last exhibit, Defendant's Exhibit 4145?

A. Yes.

Q. That is in fact a publication for peer review of the Kalso study. Is that not correct?

A. Yes. There were more than -- this is not the only publication. There was a second mentioned publication as well, of the Kalso study, by the same authors.

Q. OK.

MR. FILARDI: Your Honor, except for offering some exhibits, which I would ask if I could have the lunchtime to gather up those exhibits so we could read them into the record for admission, but I do have one, a document which was handed to me, about the Sunshine study. I don't have copies of it, but there was an issue as to date. If I may do this. I don't have copies, but I would like to put it on the screen.

Defendant's Exhibit 3924.